DEXMEDETOMIDINE PREMIX FORMULATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of and claims priority under 35 U.S.C. §120 to U.S. Ser. No. 13/678,260 filed Nov. 15, 2012, which is a continuation of U.S. Ser. No. 13/541,524 filed Jul. 3, 2012, now U.S. Pat. No. 8,338,470, which is a continuation of U.S. Ser. No. 13/343,672 filed Jan. 4, 2012, now U.S. Pat. No. 8,242,158, the contents of each of which are hereby incorporated by reference in their entireties, and to each of which priority is claimed.

1. FIELD OF THE INVENTION

The present invention relates to patient-ready, premixed formulations of dexmedetomidine, or a pharmaceutically acceptable salt thereof, that can be used, for example, in perioperative care of a patient or for sedation.

2. BACKGROUND OF THE INVENTION

Racemic 4-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole, which is known under the name medetomidine, is a selective and potent α_2-adrenoceptor agonist. Medetomidine has been used as an antihypertensive agent and as a sedative-analgesic agent. It has further been observed that this compound also possesses anxiolytic effects and can therefore be used in the treatment of general anxiety, panic disorder and various types of withdrawal symptoms.

The d-enantiomer of medetomidine, the generic name of which is dexmedetomidine, is described in U.S. Pat. No. 4,910,214 as an α_2-adrenoceptor agonist for general sedation/analgesia and the treatment of hypertension or anxiety. U.S. Pat. Nos. 5,344,840 and 5,091,402 discuss dexmedetomidine in perioperative and epidural use, respectively. For example, when used in perioperative care, dexmedetomidine can reduce the amount of anesthetic necessary to anesthetize a patient. Additionally, U.S. Pat. No. 5,304,569 discusses the use of dexmedetomidine in treating glaucoma, and U.S. Pat. No. 5,712,301 discusses the use of dexmedetomidine for preventing neurodegeneration caused by ethanol consumption. Furthermore, U.S. Pat. No. 6,716,867 discloses methods of sedating a patient while in an intensive care unit by administering dexmedetomidine, or a pharmaceutically acceptable salt thereof, to the patient.

Dexmedetomidine can be administered to a patient in a variety of ways. For example, U.S. Pat. Nos. 4,544,664 and 4,910,214 disclose the administration of dexmedetomidine via parenteral, intravenous, and oral routes. U.S. Pat. No. 4,670,455 describes intramuscular and intravenous administration, while U.S. Pat. Nos. 5,124,157 and 5,217,718 describe a method and device for administering dexmedetomidine through the skin. Additionally, U.S. Pat. No. 5,712,301 states that dexmedetomidine can be administered transmucosally.

To date, dexmedetomidine has been provided as a concentrate that must be diluted prior to administration to a patient. The requirement of a dilution step in the preparation of the dexmedetomidine formulation is associated with additional costs and inconvenience, as well as the risk of possible contamination or overdose due to human error. Thus, a dexmedetomidine formulation that avoids the expense, inconvenience, delay and risk of contamination or overdose would provide significant advantages over currently available concentrated formulations.

3. SUMMARY OF THE INVENTION

The present invention relates to premixed pharmaceutical compositions of dexmedetomidine, or a pharmaceutically acceptable salt thereof, that are formulated for administration to a patient, without the need to reconstitute or dilute the composition prior to administration. Thus, the compositions of the present invention are formulated as a premixed composition comprising dexmedetomidine.

In certain non-limiting embodiments, the premixed dexmedetomidine composition is a liquid comprising dexmedetomidine, or a pharmaceutically acceptable salt thereof, at a concentration of between about 0.05 μg/mL and about 15 μg/mL.

In other non-limiting embodiments, the premixed dexmedetomidine composition is a liquid comprising dexmedetomidine at a concentration of about 4 μg/mL.

In other non-limiting embodiments, the premixed dexmedetomidine composition comprises dexmedetomidine mixed or dissolved in a sodium chloride saline solution.

In certain embodiments, the premixed dexmedetomidine composition is disposed within a sealed container or vessel.

In certain embodiments, the dexmedetomidine composition is disposed in a container or vessel and is formulated as a premixture.

In certain embodiments, the premixed dexmedetomidine composition is disposed within a sealed container as a total volume of about 20 mL, 50 mL or 100 mL.

In certain non-limiting embodiments, the premixed dexmedetomidine composition of the present invention comprises dexmedetomidine, or a pharmaceutically acceptable salt thereof, at a concentration of between about 0.05 μg/mL and about 15 μg/mL, and sodium chloride at a concentration of between about 0.01 and about 2.0 weight percent.

In other non-limiting embodiments, the premixed dexmedetomidine composition of the present invention comprises dexmedetomidine, or a pharmaceutically acceptable salt thereof, at a concentration of about 4 μg/mL and sodium chloride at a concentration of about 0.90 weight percent.

In certain embodiments, the compositions of the present invention are formulated as a pharmaceutical composition for administration to a subject for sedation, analgesia or treatment of anxiety or hypertension.

The present invention also relates to the perioperative treatment of a patient to reduce the response of the autonomic nervous system to stimuli during an operation by administering a dexmedetomidine composition of the invention.

In other non-limiting embodiments, the dexmedetomidine compositions of the present invention can be administered as an anxiolytic analgesic to a patient. In certain embodiments, the composition can be administered as a premedication prior to an operation with or without administration of an amount of an anesthetic effective to achieve a desired level of local or general anesthesia.

In other non-limiting embodiments, the dexmedetomidine compositions of the present invention can be administered as a sedative. In certain embodiments, the composition is administered preoperatively to potentiate the effect of an anesthetic, wherein administration of the composition reduces the amount of anesthetic required to achieve a desired level of anesthesia.

In certain embodiments of the present invention, the premixed dexmedetomidine composition is administered